REMARKS

Introductory Comments:

Claims 15-40 were examined in the Office Action dated 13 September 2001. Applicants note with appreciation that the Office has withdrawn the following objections and/or rejections to the claims: **(a)** the objection to claims 25 and 26 as informal; **(b)** the rejection of claims 15-30, 33-37 and 39-40 under 35 U.S.C. §112, second paragraph as indefinite; **(c)** the rejection of claims 15, 28 and 38 under 35 U.S.C. §102(b) as unpatentable over International Publication No. WO 94/23738 to McElligott et al. ("McElligott"); and **(d)** the rejection of claims 15, 21 and 22 under 35 U.S.C. §103(a) as unpatentable over U.S. Patent No. 5,630,796 to Bellhouse et al. ("Bellhouse1") in view of U.S. Patent No. 5,486,364 to King et al. ("King") and U.S. Patent No. 4,737,366 to Gergely et al. ("Gergely").

However, the following claim rejections have been maintained: **(1)** claims 15- 20, 23-28, 37 and 40 remain rejected under 35 U.S.C. §112, first paragraph, as nonenabled; **(2)** claims 15-20, 23-27, 29-31, 33-37 and 39-40 remain rejected under 35 U.S.C. §102(b) as unpatentable over Bellhouse1; and **(3)** claims 29, 30 and 32-39 remain rejected under 35 U.S.C. §102(e) as unpatentable U.S. Patent No. 6,010,478 to Bellhouse et al. ("Bellhouse2"). In addition, claims 21, 22 and 28 are objected to as being dependent upon a rejected base claim. These remaining claim objections and/or rejections are traversed for the following reasons.

Overview of the Amendment:

Applicants, by way of this amendment, have entered minor amendments to claims 15, 29 and 37 in order to recite the invention with greater particularity. Specifically, these claims have merely been amended to now recite that the pharmaceutical preparation starting material is compacted in a press. Support for the amendments to claims 15, 29 and 37 can be found

throughout the specification and claims as originally filed. Accordingly no new matter has been entered by way of the amendments to claims 15 29 and 37, and the entry thereof is respectfully requested.

Pursuant to the Revised Notice from the USPTO, dated 13 February 2003, and entitled "Amendments May Now Be Submitted In Revised Format," the subject amendment has not been provided in both "clean version" and in "marked-up version" in conformance with 37 C.F.R. §1.121(b)(1) parts (ii) and (iii). Instead, this Preliminary Amendment includes a complete listing of all claims in the present application with an indication of the current status of each. The listing begins on a separate sheet and is captioned "CURRENT STATUS OF ALL CLAIMS IN THE APPLICATION".

The Rejections Under 35 U.S.C. §112, first paragraph:

Claims 15-20, 23-28, 37 and 40 remain rejected under 35 U.S.C. §112, first paragraph, as nonenabled. Initially, the Office acknowledges that applicants' specification is enabling for "a method for forming densified particles from a particulate pharmaceutical preparation containing a peptide or a protein or a gene construct, comprising pressing or grinding said pharmaceutical preparation to provide a compacted pharmaceutical preparation and size-reducing the compacted preparation onto densified particles ... a method for delivering [the compacted pharmaceutical preparations of the invention] to a target tissue or cell of the vertebrate subject by needleless syringe, wherein said pharmaceutical agent is a peptide ro protein ... a method of delivering a gene construct encoding an antigen to a vertebrate subject, said method comprising providing a compacted particulate preparation formed from a porous preparation ... and transdermally delivering the delivering the preparation to the vertebrate subject by needleless syringe, wherein said gene construct elicits an immune response in said vertebrate subject." Office Action at page 3. However, the Office asserts that the specification is not enabling for "other embodiments of the claims" on

the basis that: (a) it would take undue experimentation in order to carry out applicants' compaction methods apart from pressing a porous pharmaceutical preparation using a hydraulic press, tablet press or rotary press "which is an essential and critical element of the presently claimed invention" (Office Action at page 5); and (b) pharmaceutical preparations containing a gene construct may be damaged due to nicks or degradation due to the compacting process (Office Action at page 6), gene therapy was considered immature and highly unpredictable as at applicants' filing date (Office Action at page 6), there is no correlation between expression of a marker gene and a desired therapeutic result for treating a plethora of diseases (Office Action at page 7), there are known factors limiting an effective gene therapy including sub-optimal vectors, lack of long-term and stable gene expression in vivo, as well as lack of efficient gene delivery to target tissues (Office Action at page 7). Applicants respectfully traverse.

With regard to the first basis for the rejection, that is, the assertion that it would require undue experimentation to carry out applicants' compaction methods without using the essential and critical element of using a press to compact the pharmaceutical, applicants draw the Office's attention to the amendments to claims 15 and 37 wherein this feature is now part of the base claims. All of the other rejected claims (claims 16-20, 23-28 and 40) depend either directly or indirectly from these claims and thus include this same limitation. Accordingly, applicants submit that this first ground for rejection has been overcome by way of the present amendment. Reconsideration and withdrawal of the rejection of claims 15-20, 23-28, 37 and 40 under 35 U.S.C. §112, first paragraph, is thus earnestly solicited.

With regard to the second basis for the rejection, that is, that applicants' compacted pharmaceuticals can comprises a gene construct and it would require undue experimentation in order to make and use such pharmaceuticals, applicants draw the Office's attention to the claims. Applicants do not claim a method for gene therapy. Applicants do claim methods for converting existing pharmaceutical preparations into a form suitable for administration from

one of their proprietary needleless syringe delivery devices, the pharmaceuticals when present in their converted (compacted) form, and methods for delivering these compacted pharmaceuticals. The recited methods for producing the compacted pharmaceuticals entail a compaction step (using a press) and then a sizing step. The recited methods for delivering the compacted pharmaceuticals entail delivery via a needleless syringe. The composition claims entail the carrying out of the compaction methods of the invention. The Office has not disputed that these methods and compositions are enabled. This is because a detailed specification has been provided, complete with numerous working examples, all detailing how to carry out the recited invention including a variety of uses for the compacted pharmaceuticals. As set forth in the MPEP at Section 2164.01(c), "if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention."

Applicants submit that the Office has imposed an enablement requirement on applicants that has no real application to the claims at issue. In this regard, when a method or composition of matter claim is limited by a particular express use, enablement of that claim should be evaluated based on that limitation. *In re Vaeck*, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). However, in contrast, when such claims are not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement. When viewing the Office's basis for this rejection, it is obvious that under the Office's analysis, there cannot possibly be any pharmaceutical that would be suitable for gene therapy. This is because they could be damaged due to nicking or other degradations, or gene therapy was just too immature and highly unpredictable, or there is no correlation between expression of a marker gene and a desired therapeutic result for treating a plethora of diseases, or, there are known factors limiting an effective gene therapy including sub-optimal vectors, lack of long-term and stable gene expression in vivo, as well as lack of efficient gene delivery to target tissues. This is obviously incorrect. Certainly, the

Office does not assert that there are no gene therapy preparations that somehow overcame all of the Office's recited concerns!

What has happened is that applicants claimed methods, which are directed to methods for created compacted preparations from known and existing compositions, have been swept into the Office's perception that there cannot possibly be a gene therapy preparation that could work, and then summarily rejected on that basis. This is obviously an incorrect result. Both applicants and the Office know full well that as at applicants' filing date, there were numerous gene therapy pharmaceuticals that skilled artisans were administering to human subjects in various clinical trials. These skilled artisans did not share the Office's view that such preparations cannot possibly work due to nicking or other degradations, or since gene therapy was just too immature and highly unpredictable, or since there was no correlation between expression of a marker gene and a desired therapeutic result for treating a plethora of diseases, or, there were known factors limiting an effective gene therapy including sub-optimal vectors, lack of long-term and stable gene expression in vivo, as well as lack of efficient gene delivery to target tissues. The Office has argued that there could be a number of reasons why a particular gene therapy may not work as intended (e.g., there could be and likely are examples of inoperative gene therapies), and since applicants methods could be used to convert gene therapy preparations into a form suitable for delivery via a needleless syringe, applicants' claims are not properly enabled. Applicants submit that this is improper. Applicants have clearly enabled their recited methods and compositions. The skilled artisan is given applicants' detailed specification regarding how to make and use their methods throughout their entire scope. It is well within the capacity of the skilled artisan to select a gene therapy composition that has been shown to work in other studies, and then convert the same to applicants' densified compositions as taught in applicants' specification. The possibility that the skilled artisan may need to use the various tests set forth in applicants' specification in order to ensure that the compacted pharmaceuticals still operates as intended

does not constitute undue experimentation. It is well settled that satisfaction of the enablement requirement of Section 112 is not precluded by the necessity for some experimentation such as routine screening. The prohibition is against "undue" experimentation, not merely "experimentation." *In re Angstadt*, 190 USPQ 214 (CCPA 1976). Substituting different known gene therapy compositions into applicants' proven compaction methods using applicants' detailed disclosure as a guide to do so is well within the relative skill of the ordinarily skilled artisan practicing within applicants' field.

Applicants have provided sufficient guidance to the skilled artisan with respect to how to make and use applicants' claims, and are thus in full compliance with Section 112. The Office's assertion that the claims are not enabled due to the fact that there could be inoperative gene therapy compositions extant in the art bears no reasonable relationship to the question of applicants' enabling disclosure. For all of the foregoing reasons, then, the rejection of claims 15-20, 23-28, 37 and 40 under 35 U.S.C. §112, first paragraph, is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

The Rejections Under 35 U.S.C. §102:

Claims 15-20, 23-27, 29-31, 33-37 and 39-40 remain rejected under 35 U.S.C. §102(b) as unpatentable over Bellhouse1. In particular, the Office continues to equate the grinding that Bellhouse1 carried out in order to comminute pharmaceuticals into small particles, with applicants' recited compaction methods. Applicants respectfully traverse.

Initially, applicants draw the Office's attention to the amendments to claims 15, 29 and 37 tendered herewith, wherein it is now expressly recited that the starting pharmaceutical preparation is compacted using a press. The rest of the rejected claims (16-20, 23-27, 30-31, 33-36 and 40 depend either directly or indirectly from these base claims and thus include these same base limitations.

The "grinding" that the Office has referred to in Bellhouse1 is clearly used as a way to comminute a powder into smaller particles, not to increase density. Applicants likewise disclose throughout their specification that grinding is used to size reduce a compacted material, see, e.g., page 33, lines 12-15 ("when spray-dried and lyophilized pharmaceutical particles are ground or milled, they yield very small, light and non-dense particles that are poorly suited for delivery through skin or mucosal tissues"); page 11, lines 18-23 ("the resulting compacted material is then size-reduced using conventional methods"); page 12, lines 6-11 ("the densified material can then be reground"); page 31, lines 20-22 ("the resulting compacted material is then coarsely reground until visually broken up"); and page 34, lines 10-12 ("the resulting compacted material is then coarsely reground until visually broken up"). Accordingly, applicants respectfully submit that there is no reasonable argument that can be tendered that the "grinding" used by Bellhouse1 would be equivalent to the "compaction using a press" element as recited in applicants' amended claims.

Since anticipation of a claim under §102 *requires* that each and every element of the claims be inherent in, or disclosed expressly by the anticipating reference (*Constant v. Advanced Micro-Devices, Inc.*, 7 USPQ2d 1057, 1064 (Fed. Cir. 1988)), Bellhouse1 cannot anticipate applicants' claims. Reconsideration and withdrawal of the rejection of claims 15-20, 23-27, 29-31, 33-37 and 39-40 under 35 U.S.C. §102(b) is thus respectfully requested.

Claims 29, 30 and 32-39 remain rejected under 35 U.S.C. §102(e) as unpatentable over Bellhouse2. The Office asserts that Bellhouse2 is properly citable since "applicants have failed to provide the priority paper 9619002.0" and "as such, the filing date of 14 August 1997 for [Bellhouse2] qualifies it as a 102(e) reference." Office Action at page 19.

In response, applicants have tendered (as a separate submission to this response and RCE request) certified copies of all four priority documents (PCT/GB97/01636; PCT/GB97/02478; GB 9612629.7 and GB 9619002.0) to their instant application. As can be seen by a review of these documents, applicants are clearly entitled to their claimed

priority date of 11 September 1996. Accordingly Bellhouse2, with a date of 14 August 1997 is not properly available as 102(e) art, and the rejection is improper. Reconsideration and withdrawal of the rejection of claims 29, 30 and 32-39 under 35 U.S.C. §102(e) is thus respectfully requested.

The Objections to the Claims:

Claims 21-22 and 28 were objected to on the basis that they depend from rejected base claims. In response, applicants submit that the claim amendments tendered herewith, and the accompanying traversal is sufficient to overcame all pending claim rejections. Reconsideration and withdrawal of the objection to claims 21-22 and 28 is thus respectfully requested.

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CONCLUSION

Applicants submit that the claims define an invention which is both novel and nonobvious over the prior art. Accordingly, a Notice of Allowance is believed in order and the issuance of such a notice is respectfully requested. Applicants further ask that, should the Office note any minor remaining issues that may be resolved with a telephone call, that the Office contact the undersigned in the UK at +44 1865 332 600.

Respectfully submitted,

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